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3535 FIREWHEEL DR., SUITE A, FLOWER MOUND, TX 75028-2628
PHONE (972) 355-9700 FAX (972) 355-9984 TOLL FREE (888) 326-3311
E-MAIL: pwcarr@shotcarr.com
Web Page: www.shotcarr.com

January 3, 2002

SUITABILITY PETITION

Dockets Management Branch
Food and Drug Administration (HFA-305)
12420 Parklawn Drive (Room 1-23)
Rockville, MD 20857

RE: Suitability Petition

Dear Sir/Madam:

Enclosed are four copies of a suitability petition we are filing on behalf of Ambi Pharmaceuticals, Inc., Brooksville, FL 34604. The petition requests the Commissioner to permit Ambi to file an abbreviated new drug application (ANDA) for a tableted product containing hydrocodone bitartrate and acetaminophen at strengths different from the RLD drugs as defined in the attached petition.

Sincerely,

Paul W. Carr, P.E., R.A.C.
Regulatory Consultant

Enclosure

cc: Ambi Pharmaceuticals, Inc.

PWC:pbh

028-0004

CP 1

Petition Filed By:

Ambi Pharmaceuticals, Inc. (Ambi)
16206-A Flight Path Drive
Brooksville, FL 34604

Proposed Products:

Oral Tablet Dosage Forms Containing
10 mg hydrocodone bitartrate/200 mg acetaminophen
7.5 mg hydrocodone bitartrate/200 mg acetaminophen
5 mg hydrocodone bitartrate/200 mg acetaminophen

SUITABILITY PETITION

The undersigned submits this Suitability Petition under Section 505 of the Federal Food, Drug and Cosmetic Act (FFDCA) (21 U.S.C. 355(j)(2)(C), which authority has been delegated to the Commissioner of Food and Drugs under 21 CFR §5.10. Petitioner requests the Commissioner of Food and Drugs to make a determination that the drug products hereinafter described are suitable for consideration under an abbreviated new drug application (ANDA).

A. Action Requested

Ambi requests a determination that a drug product containing 200 mg acetaminophen, 10 mg hydrocodone bitartrate, a drug product containing 200 mg acetaminophen, 7.5 mg hydrocodone bitartrate, and a drug product containing 200 mg acetaminophen, 5 mg. hydrocodone bitartrate in tablet form for oral administration is suitable for evaluation under an ANDA.

We also request the Food and Drug Commissioner to grant a waiver from the requirements of a pediatric study for a change in dosage form on the basis that this combination of active ingredients is currently approved by the Food and Drug Administration at several strength combinations, all for the same disease conditions, but allows the physician to properly prescribe the appropriate strength depending on the severity of the condition. We understand the agency's desire to seek information regarding the use of this drug in various pediatric populations. However, in this case the product labeling already includes approved uses and dosing instructions for the most significant patient population. We propose that the concept of a standardized dosage adjustment for safety or efficacy, which is the usual goal of pediatric studies, is not relevant to this drug. In accordance with 21 CFR 314.55(c) the Commissioner may grant full or partial waiver of the study requirements on his own initiative **or** at the request of the applicant.

B. Statement of Grounds

The FFDCA allows an ANDA applicant to petition FDA for permission to file an ANDA for a drug product whose strength differs from that of the listed drug. See 21 U.S.C. §355(j)(2)(C); 57 Fed. Reg. 17950-17952(1992).

In the case of the proposed products there are several reference listed drug (RLD) products for tablets published in, "*Approved Drug Products with Therapeutic Equivalence Evaluations,*" (The Orange Book) covering strengths of acetaminophen from 325 mg to 750 mg along with hydrocodone strengths from 2.5 mg to 10 mg (Attachment 1). We have also attached a table listing products similar to the proposed products that have been approved or for which suitability petitions have been accepted (Attachment 2).

The proposed products are similar to the reference (RLD) products in that the proposed products contain acetaminophen and hydrocodone in combination as a proven analgesic.

The legal basis under which this application proceeds is as promulgated in the FFDCA, noted above, which allows the Commissioner to accept a generic drug application for a drug which differs in dosage strengths from the pioneer or reference drug product. The petitioner is not aware of any information that would be unfavorable to the granting of the requested action.

extraordinary circumstances exist that may significantly affect the human environment as discussed under 21 CFR 25.21.

D. Economic Impact

As provided in 21 CFR 10.30(b), economic impact information is to be submitted only when requested by the Commissioner following review of the petition.

E. Identification of RLD

Ambi is attaching labeling for the RLD product to which they are comparing the proposed drugs. These products are as follows:

Application No.	Name of Drug	Company
40288	Hydrocodone bitartrate/ Acetaminophen 5 mg/400 mg 7.5 mg/400 mg 10 mg/400 mg	Endo Pharmaceuticals, Inc.

F. Labeling

Attachment 3 provides copies of the proposed generic product labeling and Attachment 4 provides copies of the reference drug labeling. [Please note: Ambi is still in the process of finalizing the design of the product container label. We have included several styles in Attachment 3, but the text will remain the same. Lot No. and Exp. Dating will be imprinted on the labels during the labeling operations.]

Following is a description of the differences between the proposed generic product labeling and the RLD package inserts.

PACKAGE INSERT

1. Replaced "Zydone®" trade name with the Ambi trade name of "Maxi Tab".

- **Description**

    A. Replaced the trade name "Zydone" with "Maxi Tab".

    B. Change the descriptive text as follows:

FROM:

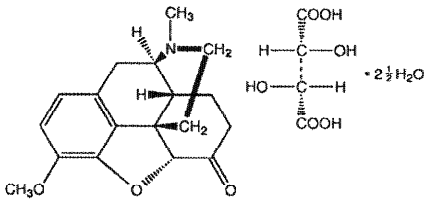
DESCRIPTION

ZYDONE Tablets for oral administration, contain hydrocodone bitartrate and acetaminophen in the following strengths:

Hydrocodone Bitartrate, USP	5 mg
Acetaminophen, USP	400 mg
Hydrocodone Bitartrate, USP	7.5 mg
Acetaminophen	400 mg
Hydrocodone Bitartrate, USP	10 mg
Acetaminophen, USP	400 mg

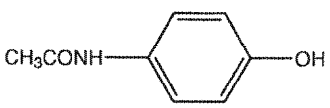
In addition, each tablet contains the following inactive ingredients: colloidal silicon dioxide, croscarmellose sodium, crospovidone, microcrystalline cellulose, povidone, pregelatinized starch, and stearic acid. The 5 mg/400 mg strength contains FD&C Yellow No. 10; 7.5 mg/400 mg contains FD&C Blue No. 2; and 10 mg/400 mg contains FD&C Red No. 40.

Hydrocodone bitartrate is an opioid analgesic and antitussive and occurs as fine, white crystals or as a crystalline powder. It is affected by light. The chemical name is: 4,5α-Epoxy-3-methoxy-17-methymorphinan-6-one tartrate (1:1) hydrate (2:5). It has the following structural formula:



$C_{18}H_{21}NO_3 \cdot C_4H_6O_6 \cdot 2\frac{1}{2}\ H_2O$ MW = 494.50

Acetaminophen, 4'-hydroxyacetanilide, a slightly bitter, white, odorless crystalline powder, is a non-opiate, non-salicylate analgesic and antipyretic. It has the following structural formula:



$C_8H_9NO_2$ MW = 151.17

TO THE FOLLOWING:

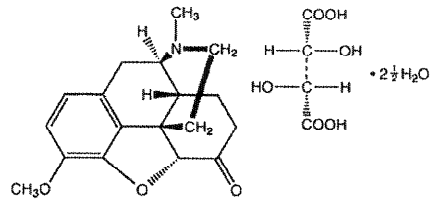
DESCRIPTION

Maxi Tab tablets, for oral administration, contain hydrocodone bitartrate and acetaminophen in the following strengths:

Hydrocodone Bitartrate, USP	5 mg
Acetaminophen, USP	200 mg
Hydrocodone Bitartrate, USP	7.5 mg
Acetaminophen, USP	200 mg
Hydrocodone Bitartrate, USP	10 mg
Acetaminophen, USP	200 mg

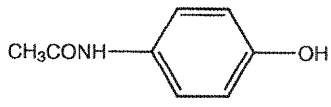
In addition, each tablet contains the following inactive ingredients: colloidal silicon dioxide, croscarmellose sodium, crospovidone, microcrystalline cellulose, povidone, pregelatinized starch, and stearic acid.

Hydrocodone bitartrate is an opioid analgesic and antitussive and occurs as fine, white crystals or as a crystalline powder. It is affected by light. The chemical name is 4,5(alpha)-Epoxy-3-methoxy-17-methylmorphinan-6-one tartrate (1:1) hydrate (2:5). It has the following structural formula:



$C_{18}H_{21}NO_3 \cdot C_4H_6O_6 \cdot 2\frac{1}{2}\ H_2O$ MW = 494.50

Acetaminophen, 4'-hydroxyacetanilide, a slightly bitter, white, odorless, crystalline powder, is a non-opiate, non-salicylate analgesic and antipyretic. It has the following structural formula:



$C_8H_9NO_2$ MW = 151.17

- **CLINICAL PHARMACOLOGY**

  No changes

- **INDICATIONS AND USAGE**

  Changed "ZYDONE" to "Maxi Tab"

- **CONTRAINDICATIONS**

  No changes

- **WARNINGS**

  No changes

- **PRECAUTIONS**

  Changed "ZYDONE" to "Maxi Tab" in all subsections

- **ADVERSE REACTIONS**

  Changed "ZYDONE" to "Maxi Tab"

- **DRUG ABUSE AND DEPENDENCE**

  Changed "ZYDONE" to "Maxi Tab"

- **OVERDOSAGE**

  Removed the registered trade name NARCAN® and left the chemical name, "naloxone hydrochloride"

- **How Supplied**

A. Changed statement from:

HOW SUPPLIED

ZYDONE (Hydrocodone Bitartrate and Acetaminophen Tablets, USP) is supplied as follows:

5 mg/400 mg
Yellow, elongated octagonal convex tablets debossed with "E" on one side and "5" on the other.

Bottles of 100	NDC 63481-668-70
Bottles of 500	NDC 63481-668-85
Unit dose package of 100 tablets	NDC 63481-668-75

7.5 mg/400 mg
Blue, elongated octagonal, convex tablets debossed with "E" on one side and "7.5" on the other.

Bottles of 100	NDC 63481-669-70
Bottles of 500	NDC 63481-669-85
Unit does package of 100 tablets	NDC 63481-669-75

10 mg/400 mg
Red, elongated octagonal, convex tablets debossed with "E" on one side and "10" on the other.

Bottles of 100	NDC 63481-698-70
Bottles of 500	NDC 63481-698-85
Unit does package of 100 tablets	NDC 63481-698-75

Store at controlled room temperature 15°-30°C (59°-86°F).

Dispense in a tight, light-resistant container as defined in the USP, with a child-resistant closure (as required).

A Schedule III Opioid. Oral prescription where permitted by State law.

ZYDONE® is a Registered Trademark of Endo Pharmaceuticals, Inc.
NARCAN® is a Registered Trademark of Endo Pharmaceuticals Inc.

6476-00/December, 1998

B. **TO READ AS FOLLOWS:**

HOW SUPPLIED

Maxi Tab (Hydrocodone Bitartrate and Acetaminophen Tablets, USP) is supplied as follows: A white, elongated octagonal, convex tablet embossed with .
[Embossment to be added later]

5 mg/200 mg

Bottles of 100	NDC XXXXXXXXX
Bottles of 500	NDC XXXXXXXXX

7.5 mg/200 mg

Bottles of 100	NDC XXXXXXXXX
Bottles of 500	NDC XXXXXXXXX

10 mg/200 mg

Bottles of 100	NDC XXXXXXXXX
Bottles of 500	NDC XXXXXXXXX

Store at controlled room temperature 15°-30°C (59°-86°F).

Dispense in a tight, light-resistant container as defined in the USP, with a child-resistant closure (as required).

A schedule III Opioid. Oral prescription where permitted by State law.

Manufactured For:
AMBI Pharmaceuticals, Inc.
Brooksville, FL 34604

Manufactured By:
PharmaFab
Grand Prairie, TX 75050

PIN ISS 12/01

Made in USA

Typed Name: Mr. Dave Ambrose

Signature: 

Title: President / CEO

Name of Petitioner: Ambi Pharmaceuticals, Inc.
Mailing Address: 16206-A Flight Path Drive
Brooksville, FL 34604

Telephone No: (352) 797-5227